UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,668	05/06/1999	JONATHAN M. GERSHONI	27/135	1117

7590 11/28/2003

BROWDY AND NEIMARK
624 NINTH STREET, N.W.
WASHINGTON, DC 20001

EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/297,668	GERSHONI ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- Th MAILING DATE of this communicati n appears on th cover sh t with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144-182* is/are pending in the application.

4a) Of the above claim(s) *157,158,171-176,178 and 180-182* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144-156,159-170,177 and 179* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

Claims 144-182 are pending.

Claims 144-156, 159-170, 177 and 179 are rejected.

Claims 157, 158, 171-176, 178 and 180-182 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 144-151, 154, 155, 156, 159-165, and 168-170 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huse et al (Science, 1989, 246: 1275-1281) in view of Stemmer et al (U.S. Patent No. 5,811,238, filed 30 November 1995).

Regarding Claim 144, Huse et al disclose a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph).

Regarding Claim 145, Huse et al disclose the method wherein step (a) comprises cutting said DNA sequence to form said plurality of DNA fragments (page 1278, left column, first full paragraph).

Regarding Claim 146, Huse et al disclose the method wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph).

Regarding Claim 149, Huse et al disclose the method wherein step (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting the ligated fragment to form said library i.e. the

light chain fragments and heavy chain fragments are each randomly ligated into vectors and then digested (page 1277, right column, last three lines-page 1278, first three lines).

Regarding Claim 150, Huse et al disclose the method wherein said expression system comprises a plurality of bacteria and step (c) comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph).

Regarding Claim 151, Huse et al disclose the method wherein said expression system comprises a plurality of phage and step (c) comprises inserting one of said library into each of said plurality of phage (page 1278, left column, first full paragraph).

Regarding Claim 156, Huse et al disclose the method wherein the single biological unit is two or more proteins which interact to form a complex i.e. the single biological unit is a light chain and a heavy chain and the light and heavy chain interact to form an antibody complex (Abstract).

Regarding Claim 159, Huse et al disclose a method of preparing a library of peptides comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph).

Regarding Claim 160, Huse et al disclose the method wherein step (a) comprises cutting said DNA sequence to form said plurality of DNA fragments (page 1278, left column, first full paragraph).

Regarding Claim 161, Huse et al disclose the method wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph).

Regarding Claim 163, Huse et al disclose the method wherein step (b) comprises randomly ligating said plurality of DNA fragments to form at least one ligated fragment and at least partially digesting the ligated fragment to form said library i.e. the light chain fragments and heavy chain fragments were each randomly ligated into vectors and then digested (page 1277, right column, last three lines-page 1278, first three lines).

Regarding Claim 164, Huse et al disclose the method wherein said expression system comprises a plurality of bacteria and step (c) comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph).

Regarding Claim 165, Huse et al disclose the method wherein said expression system comprises a plurality of phage and step (c) comprises inserting one of said library into each of said plurality of phage (page 1278, left column, first full paragraph).

Regarding Claim 169, Huse et al disclose the method wherein the single biological unit is a protein i.e. the single biological unit is an antibody and the fragments provide in (a) are fragments of the antibody (Abstract).

Regarding Claim 170, Huse et al disclose the method wherein the single biological unit is two or more proteins which interact to form a complex i.e. the single biological unit is f a light chain and a heavy chain which interact to from an antibody complex (Abstract).

However, while Huse et al discloses applying the method to antibodies, Huse does not teach applying the method to a single gene. When claim 144 states that the plurality of DNA fragments consist of fragments from a single biological unit, this is interpreted to limit the claim to a single gene.

Stemmer teaches the use of a single gene. As Stemmer notes "The initial library can consist of related sequences of diverse origin (i.e. antibodies from naive mRNA) or can be derived by any type of mutagenesis (including shuffling) of a single antibody gene. (see column 16, lines 15-18)." This is an express teaching that a single gene can be used, and in particular, that a single antibody gene with discontinuous epitopes can be used. Stemmer drives this point the examples where example 8 clearly shows application of the shuffling to a single antibody gene and example 9 applies the method to the B-lactamase gene.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Huse to apply the analysis to a single biological unit such as a single gene because Stemmer expressly teaches the desirability of using single genes as noted above, where Stemmer stated "The initial library can consist of related sequences of diverse origin (i.e. antibodies from naive mRNA) or can be derived by any type of mutagenesis (including shuffling) of a single

antibody gene. (see column 16, lines 15-18)." An ordinary practitioner would have been motivated to combine the method of Huse and Stemmer and apply it to single genes based upon the express suggestion of Stemmer. Further, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the methods of shuffling as taught by Stemmer et al to thereby eliminate the time and labor involved with DNA digestion and DNA purification following digestion for the obvious benefit of economy of time and labor.

Regarding Claim 147, Huse et al teach a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph) but they do note teach the cutting is accomplished by mechanically cutting. However, mechanical cutting of DNA was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a

similar method of identifying and producing a peptide. Specifically, Stemmer et al teach the similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are provided by mechanically cutting (Column 17, lines 30-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the mechanical shearing as taught by Stemmer et al to thereby eliminate the time and labor involved with DNA digestion and DNA purification following digestion for the obvious benefit of economy of time and labor.

Regarding Claim 148, Huse et al teach the method wherein said fragments are provide by cutting i.e. restriction digestion (page 1278, left column, first full paragraph) but they do not teach the fragments are provided by synthesis. However, synthesis of DNA fragments was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a similar method of identifying and producing a peptide. Specifically, Stemmer et al teach a similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are synthesized (Column 17, lines 48-52). It would have

been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the synthesis as taught by Stemmer et al to thereby provide fragments of known sequence and for the obvious benefit of screening known fragments for binding activity. For example, a protein having a known sequence interacts with a ligand, but the fragment of protein which interacts with the ligand is unknown. The skilled artisan would have been motivated to analyze the encoding sequence to identify fragments encoding potential binding activity and to synthesize only those specific fragments and to randomly ligate the fragments to thereby identify and produce discontinuous peptides with bind to the ligand of interest.

Regarding Claim 154, Huse et al teach the method wherein said expression system comprises a plurality of bacteria and step (c) of inserting comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph) but they do not teach the expression system is eukaryotic. However, eukaryotic expression systems were well known in the art at the time the claimed invention was made as taught by Stemmer et al who teach the similar method wherein the expression system is eukaryotic (Column 38, lines 1-42). Additionally, they teach that eukaryotic systems are preferred because the peptide produced in secreted as an intact product (Column 38, lines 5-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage expression system of Huse et al with the eukaryotic expression system as taught by Stemmer et al and to insert the library of oligonucleotides into eukaryotic vectors for expression in a eukaryotic cell to thereby express and secret intact peptides as

preferred by Stemmer et al for the obvious benefit of obtaining an intact peptide which is secreted and therefore easily purified as taught by Stemmer et al (Column 38, lines 5-10).

Regarding Claim 162, Huse et al teach a method preparing a peptide library comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) wherein said cutting is accomplished enzymatically i.e. restriction digestion (page 1278, left column, first full paragraph) but they do note teach the cutting is accomplished by mechanically cutting. However, mechanical cutting of DNA was well know in the art at the time the claimed invention was made as taught by Stemmer et al. who teach a similar method of identifying and producing a peptide. Specifically, Stemmer et al teach the similar method comprising providing a plurality of DNA fragments which appear in a DNA sequence encoding a single biological unit (i.e. antibody); creating a library of oligonucleotides by randomly rearranging said fragments (i.e. shuffling); inserting the oligonucleotides into an expression system; expressing and screening the expressed peptide (Column 5, lines 23-50) wherein the fragments are provided by

mechanically cutting (Column 17, lines 30-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the enzyme digestion of Huse et al with the mechanical shearing as taught by Stemmer et al to thereby eliminate the time and labor involved with DNA digestion and DNA purification following digestion for the obvious benefit of economy of time and labor.

Regarding Claim 168, Huse et al teach the method wherein said expression system comprises a plurality of bacteria and step (c) of inserting comprises inserting one of said library into each of said plurality of bacteria (page 1278, left column, first full paragraph) but they do not teach the expression system is eukaryotic. However, eukaryotic expression systems were well known in the art at the time the claimed invention was made as taught by Stemmer et al who teach the similar method wherein the expression system is eukaryotic (Column 38, lines 1-42). Additionally, they teach that eukaryotic systems are preferred because the peptide produced in secreted as an intact product (Column 38, lines 5-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage expression system of Huse et al with the eukaryotic expression system as taught by Stemmer et al and to insert the library of oligonucleotides into eukaryotic vectors for expression in a eukaryotic cell to thereby express and secret intact peptides as preferred by Stemmer et al for the obvious benefit of obtaining an intact peptide which is secreted and therefore easily purified, as taught by Stemmer et al (Column 38, lines 5-10).

4. Claims 152, 153, 166 and 167 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huse et al (Science, 1989, 246: 1275-1281) in view of Stemmer et al (U.S. Patent No. 5,811,238, filed 30 November 1995).Marks et al (The Journal of Biological Chemistry, 1992, 267(23): 16007-16010).

Regarding Claims 152 and 153, Huse in view of Stemmer teach a method of identifying and producing a peptide which interacts with a ligand which interacts with a discontinuous epitope of a single biological unit comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph). As noted above, Stemmer teaches the use of the single gene (see column 16, lines 15-18).

Huse in view of Stemmer do not teach the oligonucleotides are cloned into phage genes coding for a coat protein. Marks et al teach a similar method comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to

an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 16008, Fig 1 and 2) wherein the said oligonucleotides are inserted into phage genes coding for a coat protein and wherein said coat protein is pIII or pVIII (page 16008, Fig. 2). Additionally, Marks et al teach that by inserting the oligonucleotide in to the coat proteins (e.g. pIII or pVIII) multiple antibodies are displayed on each phage providing higher binding avidity thereby maintaining antibody-antigen binding during washing even for the lower-affinity binding reactions (page 16009, left column, first paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage in the method of Huse et al in view of Stemmer by inserting the oligonucleotide in to either the pIII or pVIII coat protein of filamentous phage as taught by Marks et al to thereby express multiple antibodies on each phage and increase binding avidity thereby maintaining antibody-antigen binding during washing and selection steps for the expected benefit of obtaining even lower-affinity binding reactions as taught by Marks et al (page 16009, left column, first paragraph).

Regarding Claims 166 and 167, Huse in view of Stemmer teach a method preparing a peptide library comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. Fab antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA

fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 1277, right column, first full paragraph and Fig. 1; and page 1278, left column, first full paragraph) where a single antibody gene is used (see Stemmer column 16, lines 15-18), but they do not teach the oligonucleotides are cloned into phage genes coding for a coat protein. Marks et al teach a similar method comprising: providing a plurality of DNA fragments which appear in a DNA sequence encoding said single biological unit (i.e. antibody); creating a library of oligonucleotides comprising at least two randomly ligated DNA fragments; inserting each of said oligonucleotides in to an expression system (i.e. phage); expressing the peptides encoded by the oligonucleotides; screening the expressed peptides for interaction with a ligand that interacts with a discontinuous epitope (i.e. antigen); identifying the peptide and producing the identified peptide wherein the oligonucleotides are inserted into said phage by cloning (page 16008, Fig 1 and 2) wherein the said oligonucleotides are inserted into phage genes coding for a coat protein and wherein said coat protein is pIII or pVIII (page 16008, Fig. 2). Additionally, Marks et al teach that by inserting the oligonucleotide in to the coat proteins (e.g. pIII or pVIII) multiple antibodies are displayed on each phage providing higher binding avidity thereby maintaining antibody-antigen binding during washing even for the lower-affinity binding reactions (page 16009, left column, first paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the phage in the method of Huse et al in view of Stemmer by inserting the oligonucleotide in to either the pIII or pVIII coat protein of filamentous phage as taught by Marks et al to thereby express multiple antibodies on each phage and increase binding avidity thereby maintaining antibody-antigen binding during washing and selection steps for the expected benefit of obtaining even low-affinity binding reactions as taught by Marks et al (page 16009, left column, first paragraph) and thereby produce a more complete library as desired.

Response to Arguments

5. Applicant's arguments filed October 2, 2003 have been fully considered but they are not persuasive.

Applicant argues that the 103 rejection, which relies upon Stemmer, does not teach the use of a single biological unit. No definition for this term was found within the specification and this term is susceptible to multiple interpretations. Applicant attempts to argue that an antibody is not a "single biological unit". In the absence of any definition of this term, an antibody is a single biological unit because an antibody a single biological "thing" which performs a specific function, interacting with an antigen. An antibody is a single biological unit, whether interpreted as a single type of biological molecule for which Stemmer uses a plurality of molecules or as a functional recitation of a molecule which functions in a biological way. In the absence of any definition for this term, either interpretation is reasonable and meets the claim requirements.

Applicant's entire argument relies upon a particular definition of the phrase "single biological unit". Since this phrase is susceptible to a broad variety of meanings, as discussed above, the prior art rejection is maintained.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new

telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634